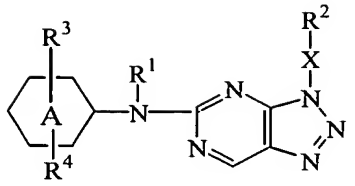
Claims

1. A compound of formula



(I),

a *N*-oxide, a pharmaceutically acceptable addition salt, a quaternary amine and a stereochemically isomeric form thereof, wherein

ring A represents phenyl, pyridyl, pyrimidinyl, pyridazinyl or pyrazinyl;

R^1 represents hydrogen; aryl; formyl; C_{1-6}alkylcarbonyl; C_{1-6}alkyl; C_{1-6}alkyloxycarbonyl; C_{1-6}alkyl substituted with formyl, C_{1-6}alkylcarbonyl, C_{1-6}alkyloxycarbonyl, C_{1-6}alkylcarbonyloxy; or C_{1-6}alkyloxyC_{1-6}alkylcarbonyl optionally substituted with C_{1-6}alkyloxycarbonyl;

X represents a direct bond; $-(CH_2)_{n3}-$ or $-(CH_2)_{n4}-X_{1a}-X_{1b}-$;

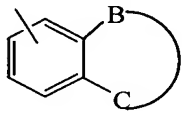
with n_3 representing an integer with value 1, 2, 3 or 4;

with n_4 representing an integer with value 1 or 2;

with X_{1a} representing O, C(=O) or NR^5; and

with X_{1b} representing a direct bond or C_{1-2}alkyl;

R^2 represents C_{3-7}cycloalkyl; phenyl; a 4, 5, 6- or 7-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N; benzoxazolyl or a radical of formula



(a-1)

wherein –B-C- represents a bivalent radical of formula

$-CH_2-CH_2-CH_2-$ (b-1);

$-CH_2-CH_2-CH_2-CH_2-$ (b-2);

$-X_1-CH_2-CH_2-(CH_2)_n-$ (b-3);

$-X_1-CH_2-(CH_2)_n-X_1-$ (b-4);

$-X_1-(CH_2)_{n'}-CH=CH-$ (b-5);

$-CH=N-X_1-$ (b-6);

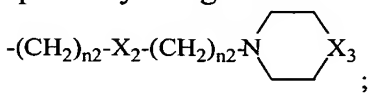
with X_1 representing O or NR^5;

n representing an integer with value 0, 1, 2 or 3;

n' representing an integer with value 0 or 1;

wherein said R^2 substituent, where possible, may optionally be substituted with at least one substituent selected from halo; hydroxy; C_{1-6}alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy,

C_{1-4}alkyloxyC_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkyl-carbonyloxy, NR^6R^7, -C(=O)-NR^6R^7, -NR^5-C(=O)-NR^6R^7, -$S(=O)_{n1}$-R^8 or -NR^5-$S(=O)_{n1}$-R^8; C_{2-6}alkenyl or C_{2-6}alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxy, NR^6R^7, -C(=O)-NR^6R^7, -NR^5-C(=O)-NR^6R^7, -$S(=O)_{n1}$-R^8 or -NR^5-$S(=O)_{n1}$-R^8; polyhalo-C_{1-6}alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, C_{1-4}alkyloxyC_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxy, NR^6R^7, -C(=O)-NR^6R^7, -NR^5-C(=O)-NR^6R^7, -$S(=O)_{n1}$-R^8 or –NR^5-$S(=O)_{n1}$-R^8; C_{1-6}alkyloxy optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyl-oxycarbonyl, C_{1-4}alkylcarbonyloxy, NR^6R^7, -C(=O)-NR^6R^7, -NR^5-C(=O)-NR^6R^7, -$S(=O)_{n1}$-R^8 or –NR^5-$S(=O)_{n1}$-R^8; polyhaloC_{1-6}alkyloxy optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, C_{1-4}alkyloxyC_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxy, NR^6R^7, -C(=O)-NR^6R^7, -NR^5-C(=O)-NR^6R^7, -$S(=O)_{n1}$-R^8 or –NR^5-$S(=O)_{n1}$-R^8; C_{1-6}alkylthio; polyhaloC_{1-6}alkylthio; C_{1-6}alkyloxycarbonyl; C_{1-6}alkylcarbonyloxy; C_{1-6}alkylcarbonyl; polyhaloC_{1-6}alkylcarbonyl; cyano; carboxyl; NR^6R^7; C(=O)NR^6R^7; -NR^5-C(=O)-NR^6R^7; -NR^5-C(=O)-R^5; -$S(=O)_{n1}$-R^8; -NR^5-$S(=O)_{n1}$-R^8; -S-CN; -NR^5-CN; aryloxy; arylthio; arylcarbonyl; arylC_{1-4}alkyl; arylC_{1-4}alkyloxy; a 5-or 6-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N and said 5-or 6-membered monocyclic heterocycle optionally being substituted with at least one substituent selected from R^9; or



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with n2 representing an integer with value 0, 1, 2, 3 or 4;
with X_2 representing O, NR^5 or a direct bond;
with X_3 representing O, CH_2, CHOH, CH-$N(R^5)_2$, NR^5 or N-C(=O)-C_{1-4}alkyl;

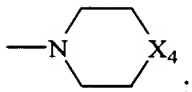
R^3 represents halo; hydroxy; C_{1-6}alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, C_{1-4}alkyloxy-C_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxy, $NR^{6b}R^{7b}$, -C(=O)-$NR^{6b}R^{7b}$, -NR^5-C(=O)-$NR^{6b}R^{7b}$, -$S(=O)_{n1}$-R^{8a} or –NR^5-$S(=O)_{n1}$-R^{8a}; C_{2-6}alkenyl or C_{2-6}alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxy, $NR^{6b}R^{7b}$,

-C(=O)-$NR^{6b}R^{7b}$, -NR^5-C(=O)-$NR^{6b}R^{7b}$, -$S(=O)_{n1}$-R^{8a} or –NR^5-$S(=O)_{n1}$-R^{8a}; polyhaloC_{1-6}alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, C_{1-4}alkyloxy-C_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxy, $NR^{6b}R^{7b}$, -C(=O)-$NR^{6b}R^{7b}$, -NR^5-C(=O)-$NR^{6b}R^{7b}$, -$S(=O)_{n1}$-R^{8a} or –NR^5-$S(=O)_{n1}$-R^{8a}; C_{1-6}alkyloxy optionally substituted with one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxy-carbonyl, C_{1-4}alkylcarbonyloxy, $NR^{6b}R^{7b}$, -C(=O)-$NR^{6b}R^{7b}$, -NR^5-C(=O)-$NR^{6b}R^{7b}$, -$S(=O)_{n1}$-R^{8a} or –NR^5-$S(=O)_{n1}$-R^{8a}; polyhaloC_{1-6}alkyloxy optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, C_{1-4}alkyloxyC_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxy, $NR^{6b}R^{7b}$, -C(=O)-$NR^{6b}R^{7b}$, -NR^5-C(=O)-$NR^{6b}R^{7b}$, -$S(=O)_{n1}$-R^{8a} or –NR^5-$S(=O)_{n1}$-R^{8a}; C_{1-6}alkylthio; polyhaloC_{1-6}alkylthio; C_{1-6}alkyloxycarbonyl; C_{1-6}alkylcarbonyloxy; C_{1-6}alkylcarbonyl; polyhalo-C_{1-6}alkylcarbonyl; cyano; carboxyl; aryloxy; arylthio; arylcarbonyl; $NR^{6b}R^{7b}$; C(=O)-$NR^{6b}R^{7b}$; -NR^5-C(=O)-$NR^{6b}R^{7b}$; -NR^5-C(=O)-R^5; -$S(=O)_{n1}$-R^{8a}; –NR^5-$S(=O)_{n1}$-R^{8a}; -S-CN; or -NR^5-CN;

R^4 represents hydrogen; halo; hydroxy; C_{1-4}alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxy, $NR^{10}R^{11}$, -C(=O)-$NR^{10}R^{11}$, -NR^5-C(=O)-$NR^{10}R^{11}$, -$S(=O)_{n1}$-R^{12} or –NR^5-$S(=O)_{n1}$-R^{12}; C_{2-4}alkenyl or C_{2-4}alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxy, $NR^{10}R^{11}$, -C(=O)-$NR^{10}R^{11}$, -NR^5-C(=O)-$NR^{10}R^{11}$, -$S(=O)_{n1}$-R^{12} or –NR^5-$S(=O)_{n1}$-R^{12}; polyhaloC_{1-3}alkyl; C_{1-4}alkyloxy optionally substituted with carboxyl; polyhaloC_{1-3}alkyloxy; C_{1-4}alkylthio; polyhaloC_{1-3}alkylthio; C_{1-4}alkyloxycarbonyl; C_{1-4}alkylcarbonyloxy; C_{1-4}alkylcarbonyl; polyhaloC_{1-4}alkylcarbonyl; nitro; cyano; carboxyl; $NR^{10}R^{11}$; C(=O)$NR^{10}R^{11}$; -NR^5-C(=O)-$NR^{10}R^{11}$; -NR^5-C(=O)-R^5; -$S(=O)_{n1}$-R^{12}; –NR^5-$S(=O)_{n1}$-R^{12}; -S-CN; or -NR^5-CN;

R^5 represents hydrogen; C_{1-4}alkyl or C_{2-4}alkenyl;

R^6 and R^7 each independently represent hydrogen; cyano; C_{1-6}alkylcarbonyl optionally substituted with C_{1-4}alkyloxy or carboxyl; C_{1-6}alkyloxycarbonyl; C_{3-7}cycloalkylcarbonyl; adamantanylcarbonyl; C_{1-4}alkyloxyC_{1-4}alkyl; C_{1-4}alkyl substituted with C_{1-4}alkyl-NR^5-; C_{1-6}alkyl optionally substituted with at least one substituent selected from halo, hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, polyhalo-

C_{1-4}alkyl, C_{1-4}alkyloxyC_{1-4}alkyloxy, $NR^{6a}R^{7a}$, $C(=O)NR^{6a}R^{7a}$ or  ; with X_4 representing O, CH_2, CHOH, CH-$N(R^5)_2$, NR^5 or N-$C(=O)$-C_{1-4}alkyl;

R^{6a} and R^{7a} each independently represent hydrogen; C_{1-4}alkyl; C_{1-4}alkylcarbonyl or a 5- or 6-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N;

R^{6b} and R^{7b} each independently represent hydrogen; cyano; C_{1-6}alkylcarbonyl optionally substituted with C_{1-4}alkyloxy or carboxyl; C_{1-6}alkyloxycarbonyl; C_{3-7}cycloalkyl-carbonyl; adamantanylcarbonyl; C_{1-4}alkyloxyC_{1-4}alkyl; C_{1-4}alkyl substituted with C_{1-4}alkyl-NR^5-; C_{1-6}alkyl optionally substituted with at least one substituent selected from halo, hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, polyhaloC_{1-4}alkyl, C_{1-4}alkyloxy-C_{1-4}alkyloxy, $NR^{6c}R^{7c}$ or $C(=O)NR^{6c}R^{7c}$;

R^{6c} and R^{7c} each independently represent hydrogen; C_{1-4}alkyl or C_{1-4}alkylcarbonyl;

R^8 represents C_{1-4}alkyl optionally substituted with hydroxy; polyhaloC_{1-4}alkyl or NR^6R^7;

R^{8a} represents C_{1-4}alkyl optionally substituted with hydroxy; polyhaloC_{1-4}alkyl or $NR^{6b}R^{7b}$;

R^9 represents halo; hydroxy; C_{1-6}alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxy, NR^6R^7, -$C(=O)$-NR^6R^7, -NR^5-$C(=O)$-NR^6R^7, -$S(=O)_{n1}$-R^8 or -NR^5-$S(=O)_{n1}$-R^8; C_{2-6}alkenyl or C_{2-6}alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxy, NR^6R^7, -$C(=O)$-NR^6R^7, -NR^5-$C(=O)$-NR^6R^7, -$S(=O)_{n1}$-R^8 or -NR^5-$S(=O)_{n1}$-R^8; polyhaloC_{1-6}alkyl; C_{1-6}alkyloxy optionally substituted with carboxyl; polyhaloC_{1-6}alkyloxy; C_{1-6}alkylthio; polyhaloC_{1-6}alkylthio; C_{1-6}alkyloxycarbonyl; C_{1-6}alkylcarbonyloxy; C_{1-6}alkylcarbonyl; cyano; carboxyl; NR^6R^7; $C(=O)NR^6R^7$; -NR^5-$C(=O)$-NR^6R^7; -NR^5-$C(=O)$-R^5; -$S(=O)_{n1}$-R^8; -NR^5-$S(=O)_{n1}$-R^8; -S-CN; or -NR^5-CN;

R^{10} and R^{11} each independently represent hydrogen; C_{1-6}alkyl; cyano; C_{1-6}alkylcarbonyl; C_{1-4}alkyloxyC_{1-4}alkyl; or C_{1-4}alkyl substituted with C_{1-4}alkyl-NR^5-;

R^{12} represents C_{1-4}alkyl or $NR^{10}R^{11}$;

n1 represents an integer with value 1 or 2;

aryl represents phenyl or phenyl substituted with at least one substituent selected from halo, C_{1-6}alkyl, C_{3-7}cycloalkyl, C_{1-6}alkyloxy, cyano, nitro, polyhaloC_{1-6}alkyl or polyhaloC_{1-6}alkyloxy.

2. A compound according to claim 1 wherein

X represents a direct bond; $-(CH_2)_{n3}-$ or $-(CH_2)_{n4}-X_a-X_b-$;

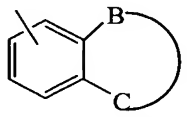
with n_3 representing an integer with value 1, 2, 3 or 4;

with n_4 representing an integer with value 1 or 2;

with X_a representing O or NR^5; and

with X_b representing a direct bond or C_{1-2}alkyl;

R^2 represents C_{3-7}cycloalkyl; phenyl or a 4, 5, 6- or 7-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N; or a radical of formula



(a-1)

wherein –B-C- represents a bivalent radical of formula

$-CH_2-CH_2-CH_2-$ (b-1);

$-CH_2-CH_2-CH_2-CH_2-$ (b-2);

$-X_1-CH_2-CH_2-(CH_2)_n-$ (b-3);

$-X_1-CH_2-(CH_2)_n-X_1-$ (b-4);

$-X_1-(CH_2)_{n'}-CH=CH-$ (b-5);

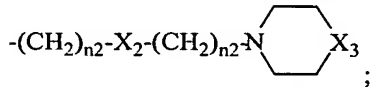
with X_1 representing O or NR^5;

n representing an integer with value 0, 1, 2 or 3;

n' representing an integer with value 0 or 1;

wherein said R^2 substituent, where possible, may optionally be substituted with at least one substituent selected from halo; hydroxy; C_{1-6}alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxy, NR^6R^7, $-C(=O)-NR^6R^7$, $-NR^5-C(=O)-NR^6R^7$, $-S(=O)_{n1}-R^8$ or $-NR^5-S(=O)_{n1}-R^8$; C_{2-6}alkenyl or C_{2-6}alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxy, NR^6R^7, $-C(=O)-NR^6R^7$, $-NR^5-C(=O)-NR^6R^7$, $-S(=O)_{n1}-R^8$ or $-NR^5-S(=O)_{n1}-R^8$; polyhaloC_{1-6}alkyl; C_{1-6}alkyloxy optionally substituted with carboxyl; polyhaloC_{1-6}alkyloxy; C_{1-6}alkylthio; polyhaloC_{1-6}alkylthio; C_{1-6}alkyloxycarbonyl; C_{1-6}alkylcarbonyloxy; C_{1-6}alkylcarbonyl; polyhaloC_{1-6}alkylcarbonyl; cyano; carboxyl; NR^6R^7; $C(=O)NR^6R^7$; $-NR^5-C(=O)-NR^6R^7$; $-NR^5-C(=O)-R^5$; $-S(=O)_{n1}-R^8$; $-NR^5-S(=O)_{n1}-R^8$; -S-CN; $-NR^5-CN$; aryloxy; arylthio; arylcarbonyl; arylC_{1-4}alkyl; arylC_{1-4}alkyloxy; a 5-or 6-membered monocyclic heterocycle containing at least one heteroatom

selected from O, S or N and said 5-or 6-membered monocyclic heterocycle optionally being substituted with at least one substituent selected from R^9; or

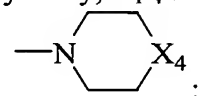


;

with n2 representing an integer with value 0, 1, 2, 3 or 4;
with X_2 representing O, NR^5 or a direct bond;
with X_3 representing O or NR^5;

R^3 represents halo; hydroxy; C_{1-6}alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxy, $NR^{6b}R^{7b}$, $-C(=O)-NR^{6b}R^{7b}$, $-NR^5-C(=O)-NR^{6b}R^{7b}$, $-S(=O)_{n1}-R^{8a}$ or $-NR^5-S(=O)_{n1}-R^{8a}$; C_{2-6}alkenyl or C_{2-6}alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxy, $NR^{6b}R^{7b}$, $-C(=O)-NR^{6b}R^{7b}$, $-NR^5-C(=O)-NR^{6b}R^{7b}$, $-S(=O)_{n1}-R^{8a}$ or $-NR^5-S(=O)_{n1}-R^{8a}$; polyhaloC_{1-6}alkyl; C_{1-6}alkyloxy optionally substituted with carboxyl; polyhaloC_{1-6}alkyloxy; C_{1-6}alkylthio; polyhaloC_{1-6}alkylthio; C_{1-6}alkyloxycarbonyl; C_{1-6}alkylcarbonyloxy; C_{1-6}alkyl-carbonyl; polyhaloC_{1-6}alkylcarbonyl; nitro; cyano; carboxyl; $NR^{6b}R^{7b}$; $C(=O)NR^{6b}R^{7b}$; $-NR^5-C(=O)-NR^{6b}R^{7b}$; $-NR^5-C(=O)-R^5$; $-S(=O)_{n1}-R^{8a}$; $-NR^5-S(=O)_{n1}-R^{8a}$; -S-CN; or $-NR^5-CN$;

R^5 represents hydrogen or C_{1-4}alkyl;

R^6 and R^7 each independently represent hydrogen; cyano; C_{1-6}alkylcarbonyl; C_{1-4}alkyloxyC_{1-4}alkyl; C_{1-4}alkyl substituted with C_{1-4}alkyl-NR^5-; C_{1-6}alkyl optionally substituted with hydroxy, C_{1-4}alkyloxy, C_{1-4}alkyloxyC_{1-4}alkyloxy, $NR^{6a}R^{7a}$, $C(=O)NR^{6a}R^{7a}$ or  ; with X_4 representing O or NR^5;

R^{6a} and R^{7a} each independently represent hydrogen; C_{1-4}alkyl; C_{1-4}alkylcarbonyl or a 5- or 6-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N;

R^{6b} and R^{7b} each independently represent hydrogen; cyano; C_{1-6}alkylcarbonyl; C_{1-4}alkyloxyC_{1-4}alkyl; C_{1-4}alkyl substituted with C_{1-4}alkyl-NR^5-; C_{1-6}alkyl optionally substituted with hydroxy, C_{1-4}alkyloxy, C_{1-4}alkyloxyC_{1-4}alkyloxy, $NR^{6a}R^{7a}$ or $C(=O)NR^{6a}R^{7a}$;

R^8 represents C_{1-4}alkyl, polyhaloC_{1-4}alkyl or NR^6R^7;

R^{8a} represents C_{1-4}alkyl, polyhaloC_{1-4}alkyl or $NR^{6b}R^{7b}$.

3. A compound as claimed in claim 1 wherein ring A represents phenyl or pyridyl; R^1 represents hydrogen; X represents a direct bond or -$(CH_2)_{n3}$-; R^2 represents phenyl or a radical of formula (b-4), wherein said R^2 may optionally be substituted with at least one substituent, in particular 1, 2 or 3 substituents, selected from halo; C_{1-6}alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, NR^6R^7, $C(=O)NR^6R^7$, C_{1-4}alkyloxy or C_{1-4}alkyloxyC_{1-4}alkyloxy; C_{1-6}alkyloxy; C_{1-6}alkyloxycarbonyl; C_{1-4}alkyloxyC_{1-6}alkyloxy; cyano; carboxyl; $C(=O)NR^6R^7$; -$S(=O)_{n1}$-R^8; arylC_{1-4}alkyloxy; or a 5-or 6-membered heterocycle containing at least one heteroatom selected from O, S or N and said 5-or 6-membered heterocycle optionally being substituted with at least one substituent selected from R^9; R^3 represents halo; hydroxy; C_{1-6}alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, $NR^{6b}R^{7b}$ or $C(=O)NR^{6b}R^{7b}$; C_{2-6}alkenyl optionally substituted with at least one substituent selected from carboxyl or C_{1-4}alkyl-oxycarbonyl; polyhaloC_{1-6}alkyloxy; C_{1-6}alkyloxy optionally substituted with C_{1-4}alkyloxy; C_{1-6}alkylthio; C_{1-6}alkyloxycarbonyl; C_{1-6}alkylcarbonyl; cyano; carboxyl; $NR^{6b}R^{7b}$; $C(=O)NR^{6b}R^{7b}$; -NR^5-C(=O)-R^5; -$S(=O)_{n1}$-R^8; -NR^5-$S(=O)_{n1}$-R^8; or -S-CN;

R^4 represents hydrogen; halo; C_{1-6}alkyl; cyano; hydroxy; C_{1-6}alkyloxycarbonyl; C_{1-6}alkyloxy; carboxyl; or NR^6R^7.

4. A compound as claimed in claim 1 or 3 wherein ring A represents phenyl or pyridyl; R^1 represents hydrogen; X represents a direct bond; R^2 represents phenyl wherein said R^2 may optionally be substituted with at least one substituent, in particular 1, 2 or 3 substituents, selected from halo; C_{1-6}alkyl substituted with one substituent selected from hydroxy, cyano, NR^6R^7, $C(=O)NR^6R^7$, C_{1-4}alkyloxy or C_{1-4}alkyloxyC_{1-4}alkyloxy; C_{1-6}alkyloxy; C_{1-6}alkyloxycarbonyl; C_{1-4}alkyloxyC_{1-6}alkyloxy; $C(=O)NR^6R^7$; -$S(=O)_{n1}$-R^8; or a 5-or 6-membered heterocycle containing at least one heteroatom selected from O, S or N and said 5-or 6-membered heterocycle optionally being substituted with at least one substituent selected from R^9; R^3 represents halo; hydroxy; C_{1-6}alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, $NR^{6b}R^{7b}$ or $C(=O)NR^{6b}R^{7b}$; C_{2-6}alkenyl optionally substituted with at least one substituent selected from carboxyl or C_{1-4}alkyloxycarbonyl; polyhaloC_{1-6}alkyloxy; C_{1-6}alkyloxy optionally substituted with C_{1-4}alkyloxy or $NR^{6b}R^{7b}$; C_{1-6}alkylthio; C_{1-6}alkyloxycarbonyl; C_{1-6}alkylcarbonyl; cyano; carboxyl; $NR^{6b}R^{7b}$; $C(=O)NR^{6b}R^{7b}$; -$S(=O)_{n1}$-R^8; -NR^5-C(=O)-R^5; or -NR^5-$S(=O)_{n1}$-R^8; R^4 represents hydrogen; halo; C_{1-6}alkyl; hydroxy; C_{1-6}alkyl-oxycarbonyl; C_{1-6}alkyloxy; carboxyl; or NR^6R^7.

5. A compound as claimed in any one of claims 1 to 4 wherein the R^3 substituent is linked to ring A in meta position compared to the NR^1 linker.

6. A compound as claimed in any one of claims 1 to 4 wherein the R^3 substituent is linked to ring A in para position compared to the NR^1 linker.

7. A compound as claimed in any one of claims 1 to 6 wherein R^3 represents $NR^{6b}R^{7b}$.

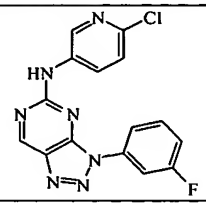
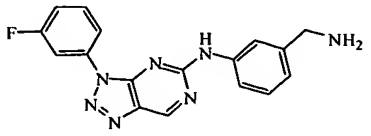
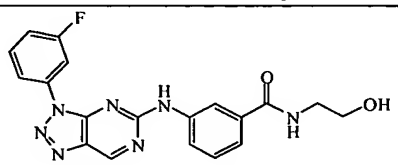
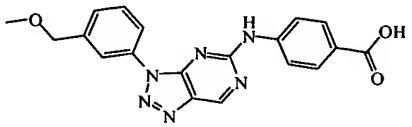
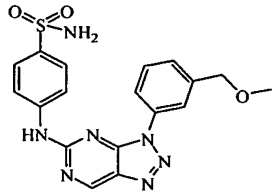
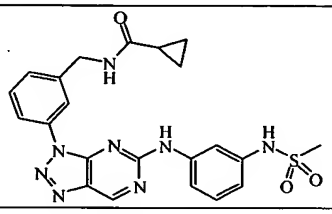
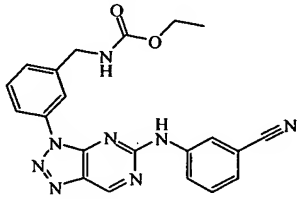
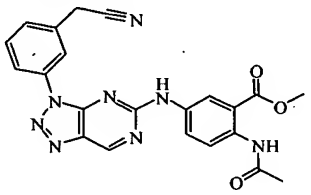
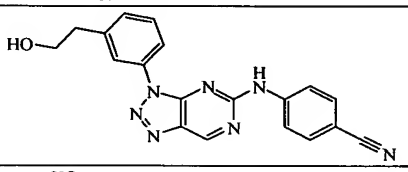
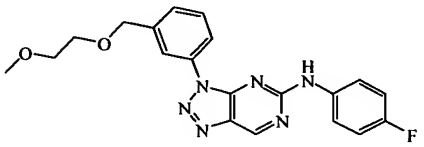
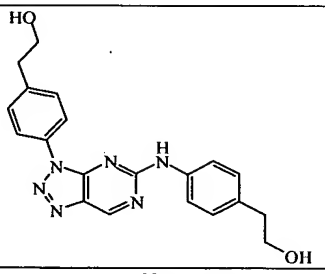
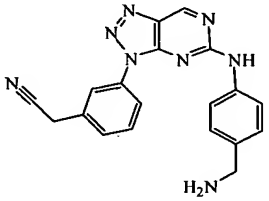
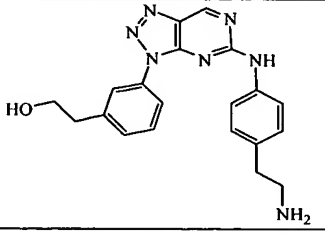
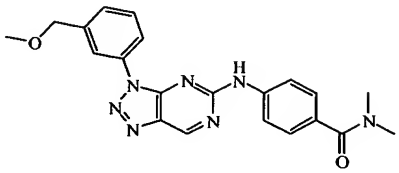
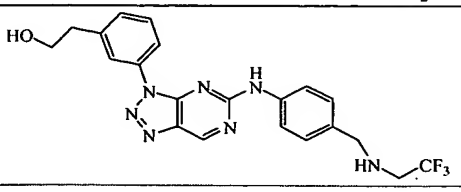
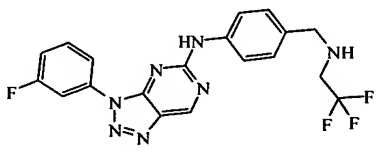
8. A compound as claimed in any one of claims 1 to 7 wherein X represents a direct bond.

9. A compound as claimed in any one of claims 1, 5 to 8 wherein R^2 represents C_{3-7}cycloalkyl; phenyl; a 4, 5, 6- or 7-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N; benzoxazolyl or a radical of formula (a-1) wherein said R^2 substituent is substituted with at least one substituent selected from C_{1-6}alkyl substituted with NR^6R^7; C_{2-6}alkenyl or C_{2-6}alkynyl, each substituted with NR^6R^7; polyhaloC_{1-6}alkyl substituted with NR^6R^7; C_{1-6}alkyloxy substituted with NR^6R^7; polyhaloC_{1-6}alkyloxy substituted with NR^6R^7; or NR^6R^7.

10. A compound as claimed in any one of claims 1, 5, 6, 8 or 9 wherein R^3 represents C_{1-6}alkyl substituted with $NR^{6b}R^{7b}$; C_{2-6}alkenyl or C_{2-6}alkynyl, each substituted with $NR^{6b}R^{7b}$; polyhaloC_{1-6}alkyl substituted with $NR^{6b}R^{7b}$; C_{1-6}alkyloxy substituted with $NR^{6b}R^{7b}$; polyhaloC_{1-6}alkyloxy substituted with $NR^{6b}R^{7b}$; or $NR^{6b}R^{7b}$.

11. A compound as claimed in any one of claims 1, 5, 6, 7, 8 or 10 wherein R^2 represents C_{3-7}cycloalkyl; phenyl; a 4, 5, 6- or 7-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N; benzoxazolyl or a radical of formula (a-1), wherein said R^2 substituent is substituted with at least one substituent selected from halo; polyhaloC_{1-6}alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, C_{1-4}alkyloxy-C_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxy, NR^6R^7, -C(=O)-NR^6R^7, -NR^5-C(=O)-NR^6R^7, -$S(=O)_{n1}$-R^8 or –NR^5-$S(=O)_{n1}$-R^8; polyhalo-C_{1-6}alkyloxy optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4}alkyloxy, C_{1-4}alkyloxyC_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxy, NR^6R^7, -C(=O)-NR^6R^7, -NR^5-C(=O)-NR^6R^7, -$S(=O)_{n1}$-R^8 or –NR^5-$S(=O)_{n1}$-R^8.

12. A compound as claimed in claim 1 wherein the compound is selected from

a *N*-oxide, a pharmaceutically acceptable addition salt, a quaternary amine and a stereochemically isomeric form thereof.

13. A compound as claimed in any one of claims 1 to 12 for use as a medicine.

14. The use of a compound as defined in any one of claims 1 to 12 for the manufacture of a medicament for the prevention or the treatment of diseases mediated through GSK3.

15. The use of a compound as defined in any one of claims 1 to 12 for the manufacture of a medicament for the prevention or the treatment of bipolar disorder (in particular manic depression), diabetes, Alzheimer's disease, leukopenia, FTDP-17 (Fronto-temporal dementia associated with Parkinson's disease), cortico-basal degeneration, progressive supranuclear palsy, multiple system atrophy, Pick's disease, Niemann Pick's disease type C, Dementia Pugilistica, dementia with tangles only, dementia with tangles and calcification, Downs syndrome, myotonic dystrophy, Parkinsonism-dementia complex of Guam, aids related dementia, Postencephalic Parkinsonism, prion diseases with tangles, subacute sclerosing panencephalitis, frontal lobe degeneration (FLD), argyrophilic grains disease, subacute sclerotizing panencephalitis (SSPE) (late complication of viral infections in the central nervous system), inflammatory diseases, depression, cancer, dermatological disorders, neuroprotection, schizophrenia, pain.

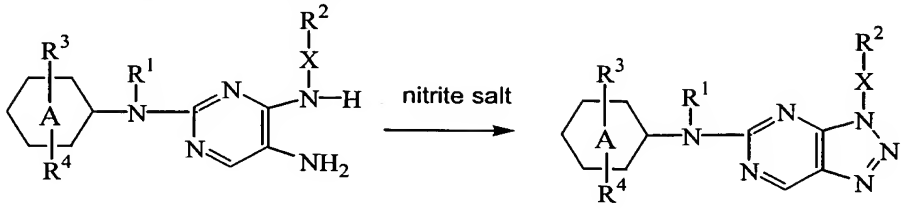
16. The use of a compound as claimed in claim 14 for the prevention or the treatment of Alzheimer's disease; diabetes; cancer; inflammatory diseases; bipolar disorder; depression; pain.

17. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as active ingredient a therapeutically effective amount of a compound as claimed in any one of claims 1 to 12.

18. A process for preparing a pharmaceutical composition as claimed in claim 17 characterized in that a therapeutically effective amount of a compound as claimed in any one of claims 1 to 12 is intimately mixed with a pharmaceutically acceptable carrier.

19. A process for preparing a compound as claimed in claim 1, characterized by

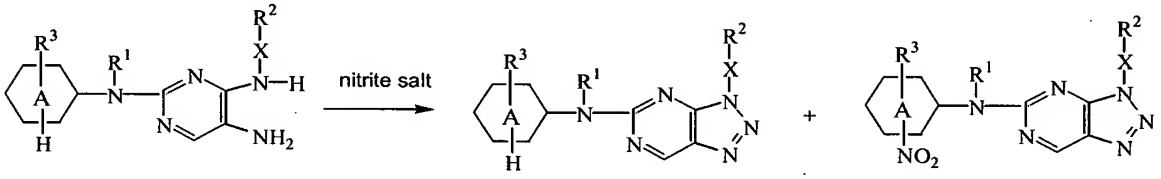
a) by cyclizing an intermediate of formula (II) in the presence of a nitrite salt, a suitable solvent, and a suitable acid,



(II) (I)

wherein ring A, R^1 to R^4 and X are as defined in claim 1;

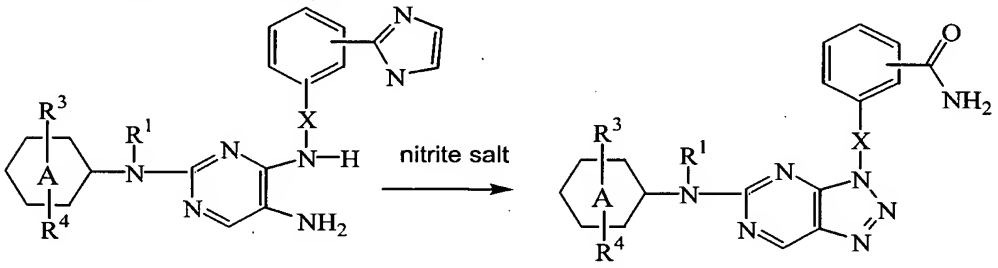
b) cyclizing an intermediate of formula (II-a) in the presence of a nitrite salt, a suitable solvent, and a suitable acid,



(II-a) (I-a) (I-b)

wherein ring A, R^1 to R^3 and X are as defined in claim 1;

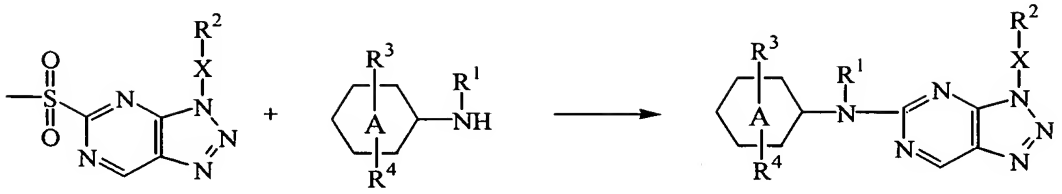
c) cyclizing an intermediate of formula (II-b) in the presence of a nitrite salt, a suitable solvent, and a suitable acid,



(II-b) (I-c)

wherein ring A, R^1, R^3, R^4 and X are as defined in claim 1;

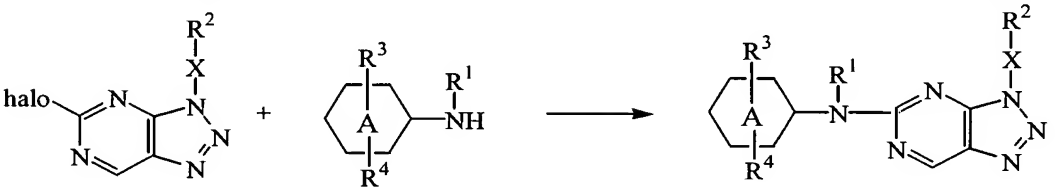
d) reacting an intermediate of formula (III) with an intermediate of formula (IV) in the presence of a suitable solvent,



(III) (IV) (I)

wherein ring A, R^1 to R^4 and X are as defined in claim 1;

e) reacting an intermediate of formula (III') with an intermediate of formula (IV) in the presence of a suitable solvent, and optionally in the presence of a suitable base,



(III') (IV) (I)

or, if desired, converting compounds of formula (I) into each other following art-known transformations, and further, if desired, converting the compounds of formula (I), into a therapeutically active non-toxic acid addition salt by treatment with an acid, or into a therapeutically active non-toxic base addition salt by treatment with a base, or conversely, converting the acid addition salt form into the free base by treatment with alkali, or converting the base addition salt into the free acid by treatment with acid; and, if desired, preparing stereochemically isomeric forms, quaternary amines or *N*-oxide forms thereof.